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CONTRIBUTION OF HYPEROXIA TO LIPID PEROXIDATION IN CORONARY ARTERY OPERATIONS: SHOULD WE KEEP A LOW OXYGEN TENSION?

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Oxygen free radicals are known to play a significant role in the morbidity associated with cardiac operations. They seem to be produced through two major pathways, heart ischemia-reperfusion[1] and leukocyte activation.[2] Another possible pathway might be the hyperoxia that occurs during cardiopulmonary bypass (CPB) and within a short period during which the patient is still supported by mechanical ventilation. The contribution of hyperoxia to oxygen free radical generation and consequent lipid peroxidation in cardiac operations has to date not been addressed. The purpose of the present study was to elucidate the role of hyperoxia in lipid peroxidation during cardiac operations.

Patients and methods. After obtaining informed consent, we entered 24 consecutive patients scheduled for routine coronary artery operation into the study. Patients in cardiogenic shock were excluded from the study. The mean age was 63.2 ± 2.1 years (range 44 to 83) and there were 17 men and 7 women. Ischemic time was 46.8 ± 3.2 minutes (range 24 to 92) CPB time 98.7 ± 5.4 minutes (range 67 to 174), and blood partial O_2 tension (Po_2) during CPB 45.4 ± 1.2 kPa (range 29 to 57). Anesthesia was instituted with fentanyl, pancuronium, and isoflurane. A membrane oxygenator (CML membrane hollow-fiber oxygenator, Cobe Inc., Lakewood, Colo.) was used for extracorporeal circulation and pH management was done with the pH-stat method. Myocardial protection was achieved with the use of intermittent fibrillation. The nasopharyngeal temperature was maintained at approximately 32° C during the CPB period. No patient received drugs known specifically to scavenge free radicals (allopurinol, mannitol, captopril, and desferrioxamine). Anesthetists and perfusionists responsible for controlling the degree of oxygenation were blind to the study.

Peripheral venous blood samples for determination of whole plasma hydroperoxide concentrations (WPHC) were obtained before the operation and 1, 6, 24, and 72 hours after CPB was discontinued. The venous blood samples were drawn into vacuum tubes containing dry lithium-heparin, placed immediately on ice, and the plasma separated on a centrifuge (4° C, 3000 rpm, 10 minutes) within 30 minutes. The separated plasma was then immediately frozen to −75° C until assayed. WPHC were measured with use of the Peroxoquant kit (lipid compatible formulation) purchased from Pierce & Warriner Ltd., Chester, United Kingdom. Arterial blood samples for determination of blood gas values were obtained from the radial artery at the corresponding times (288 blood gas system, Ciba-Corning, Inc., Medfield, Mass.).

Data were analyzed with the Statgraphics statistical program (Statgraphics, version 6.0, Manugistics, Inc., Rockville, Md.). Two-way analysis of variance was used to describe changes over time. Linear, nonlinear, and multiple regression analyses were used to identify relationships between WPHC, Po_2, and other related variables. Results were expressed as mean plus or minus standard error and differences were considered significant at a probability level of p less than 0.05.

Results. No patient received inotropic support during or after the operation and none of them had any significant complication during the 72 hours of observation. Time changes of WPHC and Po_2 values are presented in Fig. 1. The WPHC 1 hour after CPB was related to neither Po_2 at the corresponding time nor mean Po_2 during CPB ($p = 0.44$, $r = -0.16$ and $p = 0.37$, $r = -0.19$, respectively). Multiple regression analysis showed that Po_2 levels during CPB did not influence the WPHC 1 hour after CPB, even when CPB time was taken into account (Table I).

Discussion. Lipid peroxidation, although absent during CPB, has been shown to be present in the first few hours after its discontinuation.[3] Hyperoxia, which is known to increase the formation rate of oxygen free radicals (superoxide, hydrogen peroxide, and hydroxyl radical) and lipid peroxides,[4] is present during and for several hours after CPB. In this study significant hyperoxia, almost four times the baseline value, occurred during

Table I. *Multiple regression analysis for WPHC 1 hour after CPB*

	Coefficient	*SE*	*p Value*
Dependent variable			
WPHC 1 hour after CPB			
Independent variables			
mean Po_2 during CPB	−0.14	0.18	0.43
CPB time	0.04	0.04	0.34

p Value for the full regression = 0.43. *SE,* Standard error.

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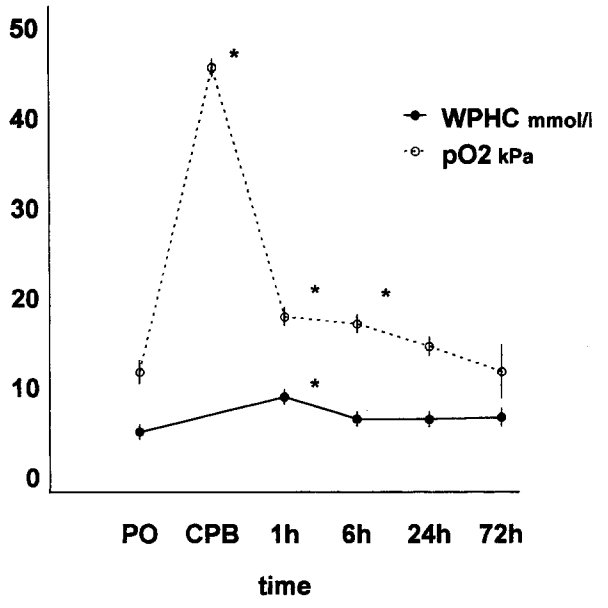

Fig. 1. Time changes of WPHC and Po_2 values in coronary artery operations undertaken with CPB. Results are expressed as mean and standard error. *PO,* Preoperative; *, statistically significant difference from baseline value.

CPB and persisted at lower levels for at least 24 hours after the operation. Plasma hydroperoxide concentration, an index of lipid peroxidation with high precision,[5] was found to increase only 1 hour after CPB and had returned to the normal range after 6 hours. Furthermore, the degree of hyperoxia during and after CPB was not found to be related to the levels of lipid peroxidation. This lack of relationship persisted even when the CPB time, an index of the duration of exposure to hyperoxia, was taken into account.

In conclusion, early post-CPB lipid peroxidation cannot be explained by the degree or the duration of hyperoxia alone, and therefore ischemia-reperfusion, leukocyte activation, and antioxidant defense system impairment may remain the major pathogenic mechanisms. Thus attempts to reduce the high Po_2 levels during cardiac operations, to protect from oxygen free radical damage, may not be vital. More aggressive measures with antioxidant supplementation may be more important.

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